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(71) Applicant *(for all designated States except US)*: CARRI-MED LTD. [GB/GB]; Carri-Med House, Glebelands Centre, Vincent Lane, Dorking, Surrey RH4 3YX (GB).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)* : KAYE, Paul, Henry [GB/GB]; TRACEY, Mark, Christopher [GB/GB]; Hatfield Polytechnic, College Lane, Hatfield, Herts. AL10 9AB (GB).

(74) Agent: MAURY, Richard, Philip; Sommerville & Rushton, 11 Holywell Hill, St. Albans, Herts. AL1 1EZ (GB).

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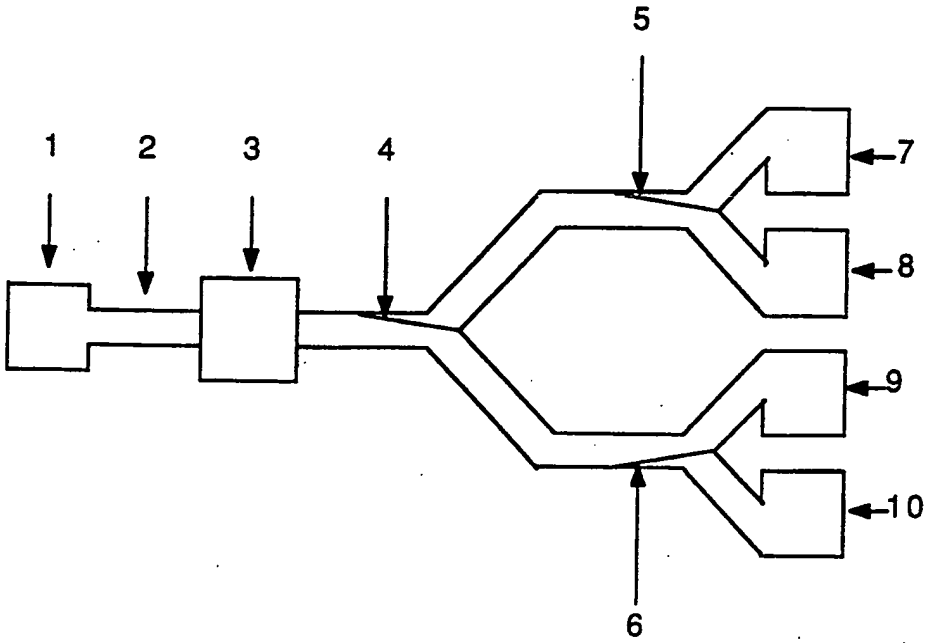
(54) Title: MICROFABRICATED DEVICE FOR BIOLOGICAL CELL SORTING



(57) Abstract

Apparatus for sorting cells into spatially separate sub-groups, comprising a microfabricated moveable structure (4, 5, 6) for directing cells between distinct spatial locations.

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Microfabricated Device for Biological Cell Sorting

This invention relates to the sorting of biological cells into spatially separate sub groups. The criteria for sorting may be applied to measurements obtained by any technique or techniques suitable for microfabricated or electronic implementation on a substrate.

Microfabrication and microelectronic techniques offer a number of actual and potential measurement techniques that may be applied to characterize biological cells. Examples of these are microrheological measurements as disclosed in International Patent Application No. PCT/GB91/00289 and morphological measurements. When suitably implemented such techniques can be applied on a cell by cell basis.

When characterizing a population of cells it can be of interest to workers to be able to isolate a sub population whose measured parameters lie within certain bounds. This could enable, for example, the culturing of a cell line from sorted cells possessing a certain property or properties of interest.

We have discovered that recent developments in

microfabrication, namely the development of controlled, deflectable, microbeams capable of deflections in the order of a few micrometres, may be used to provide the component parts of microfabricated cell sorters. Relevant microelectromechanical structures, and their formation by selective CVD techniques, are disclosed in: "Selective Chemical Vapor Deposition of Tungsten for Microelectromechanical Structures" by N.C. MACDONALD et al., Sensors and Actuators, 20 (1989) 123-133. The so-called "microtweezers" are activated by control voltages applied to electrodes.

According to the current invention such a machine is implemented by utilising a microfabricated moveable structure, preferably microfabricated beams, to direct cells between distinct spatial locations.

A particular implementation of the invention is shown in the drawing, which is a topological plan view of a substrate on which a cell sorter is formed. In this example the cells to be sorted, whose diameters may be only a few micrometres, are fed sequentially from an entry port 1, via a guiding structure 2, past a generalised sensing device or zone 3. Depending upon the result of the measurement and its interpretation the deflectable beams 4, 5, 6, are set into appropriate states to direct the cell into a particular destination,

for example, a hole 7, 8, 9 or 10 etched through the substrate. In the example shown the destination is structure 9. The beams, along with associated bifurcations can be extended to a tree structure of 'n' levels thereby yielding 2^n possible sorting sub ranges.

The absolute lengths of the channels are as short as possible while maintaining compatibility with interconnecting structures. The shafts 1, 3, 7-10 may be fabricated by selective etching as disclosed in the copending International Patent Application referred to above; the etched substrate is closed by a glass/silica cover, thereby forming the channels as tunnels.

Typical dimensions of the entry port 1 are 500μm or less square; of the sensing zone about 100 μm square; of the channels about 5 to 10μm in width and depth; of the holes (shafts) 7 - 10 about 500 μm or less square; and of the beams, which are typically of constant rectangular section, about 150μm long by 3μm square. The overall dimensions of the device could be 1cm square.

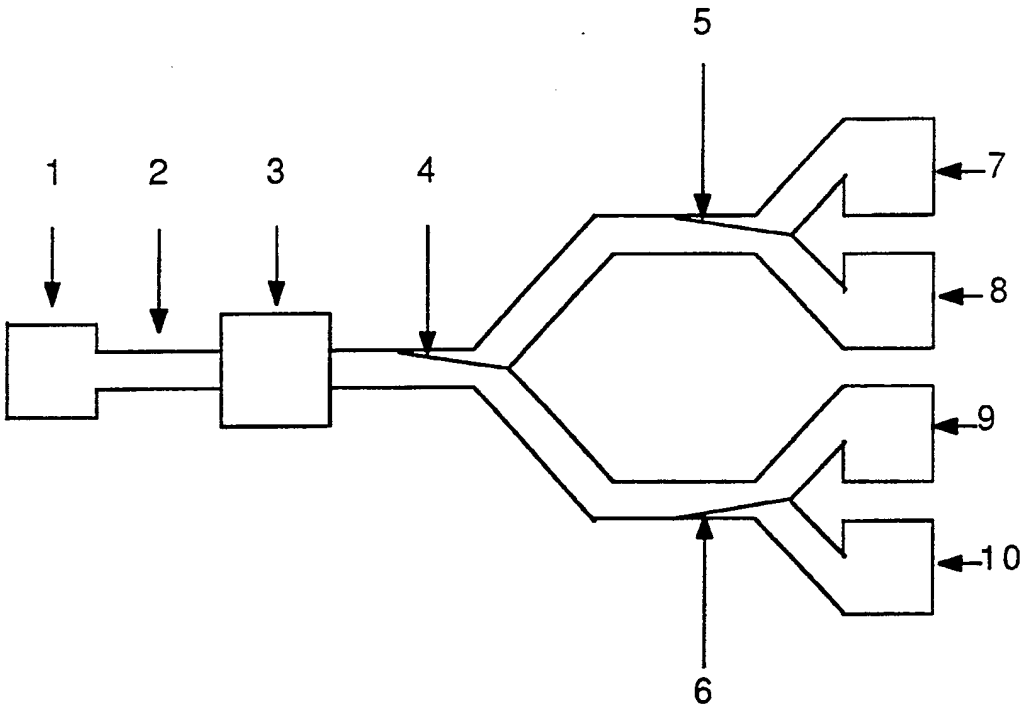
The beams are activated by selective control voltages applied as signals for control circuitry (not shown) operated, for example, under the control of a microprocessor or other computer. The computer is

programmed to control the beams' deflection in response to the desired cell-sorting procedural steps.

Claims:

1. Apparatus for sorting cells into spatially separate sub-groups, comprising a microfabricated moveable structure (4, 5, 6) for directing cells between distinct spatial locations.

2. Method for sorting cells into spatially separate sub-groups, comprising directing the cells into distinct spatial locations using a microfabricated moveable structure.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INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 91/00542

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl. 5 G01N15/14 ; G01N15/02 ; B07C5/342

II. FIELDS SEARCHED

Minimum Documentation Searched

Classification System	Classification Symbols
Int.Cl. 5	G01N ; B07C ; B01L

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched

III. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
A	US,A,4 676 274 (JAMES F BROWN) June 30, 1987 see column 9, line 22 - line 56 see column 12, line 7 - line 60; figures 12,18	1,2
A	REVIEW OF SCIENTIFIC INSTRUMENTS. vol. 51, no. 1, January 1980, NEW YORK US pages 111 - 115; P LENZ: 'Mechanical cell separator ' see page 111 - page 113	1,2
A	PROCEEDINGS OF THE IEEE. vol. 70, no. 5, May 1982, NEW YORK US pages 420 - 457; K E PETERSEN: 'Silicon as a mechanical material ' see page 434 - page 435 see page 442 - page 443 see page 446 - page 449	1,2

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
12 JULY 1991	30.07.91
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	HODSON C.M.T.

Form PCT/ISA/210 (second sheet) (January 1985)

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category °	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
A	EP,A,177 718 (PARTEC AG) April 16, 1986	

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO.

GB9100542
SA 46699

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A-4676274	30-06-87	EP-A- 0293519	07-12-88
EP-A-177718	16-04-86	CA-A- 1256825	04-07-89
		JP-A- 61137062	24-06-86
		US-A- 4756427	12-07-88